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# Lead

CAS #7439-92-1 (1)

Molecular Weight: 207.2 (1)

## Criteria and Standards

EPA Group $B_2$ Carcinogen

Cancer Potency Factor (CPF): None established due to uncertainty and importance of other health effects at low levels (2)

Reference Dose (RfD): No threshold level established, since very low levels are known to cause adverse health effects, especially in children. Current risk assessment methodology involves calculating the projected population distribution of blood lead levels associated with various exposure scenarios. (2) (15)

Maximum Contaminant Level Goal: 20 µg/l, proposed (drinking water) (2)

Maximum Contaminant Level: 50 µg/l, promulgated (drinking water) (2)

Ambient Water Quality Criteria: 50 µg/l, based on ingesting aquatic organisms and drinking water (2)

Ambient Water Quality Criteria: 50 µg/l, adjusted for drinking water only (2)

Acute Intake Chronic: $1.4 \times 10^{-3}$ mg/kg-day, oral (3)

$4.3 \times 10^{-4}$ mg/kg-day, inhalation (3)

Health Advisory: 20 µg/day (lifetime, drinking water) (3)

American Conference of Government Industrial Hygienists:

Threshold Limit Value-Time Weighed Average: 0.15 $mg/m^3$, airborne inorganic dust and fumes, as Pb (4)

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Centers for Disease Control:

Elevated Blood Lead Level for Children: 25 μg/dl (associated with a blood erythrocyte protoporphyrin level of 35 μg/dl or greater (11)

## Chemistry and Uses

Lead is a heavy metal that exists in one of three oxidation states 0, +2, and +4. Metallic lead and common lead minerals are relatively insoluble in water, however, organic lead compounds are water soluble (5). Metallic lead is used as a major component of many alloys such as solder, print-type metal, and many bronzes. Lead compounds also have a wide variety of uses as paint pigments, in storage batteriesm, and in ceramics (1).

## Pharmacokinetics

Approximately 8% of the lead ingested by human adults is thought to be absorbed. Absorption rates in children are higher, for example, children are thought to absorb as much as 45-50% of lead in foods (8). This absorption level is generally higher in animals or humans that have been fasting. The absorption rate for human infants is approximately 50%. Lead is also absorbed after inhalation; reported pulmonary deposition rates as range from 30% to 50%.

After being absorbed by the body, most lead compounds dissociate, yielding inorganic lead. Tetraethyl and tetramethyl leads are dealkylated to tri- and di- alkyl compounds which are more toxic than the parent compounds. In human adults, under conditions of long-term exposure, approximately 95% of the total amount of lead found in the body is localized in the skeleton. In the blood, most lead is found in the erythrocytes. Lead also readily crosses the placenta. In most species, the main route of excretion is through the bile. However, in baboons and humans, urine appears to be the primary route (5,8).

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## Toxicity

## Systemic Effects

## Human

At high exposure levels, lead produces encephalopathy, gastrointestinal effects, anemia, nephropathy, and electrocardiographic abnormalities. These effects are primarily seen in acutely poisoned children or in adults from occupational exposures. Lower level exposure to lead in all humans can affect the synthesis of heme, which, in turn, affects metabolic processes and decreases vitamin D circulating in the body, reducing calcium stability in the body.

Inhalation of airborne lead is generally a minor exposure pathway for children, but ingestion of lead-containing particles in dust can contribute significantly to children's lead exposure (11). Effects of great concern from low level lead exposure include neurobehavioral decrement and growth retardation in infants exposed prenatally and children exposed postnatally. Based on blood lead concentrations, no clear threshold for neurobehavioral effects has been shown from low level lead exposures resulting in blood lead levels < 10-15 μg/dl (9).

Increased blood pressure from low level lead exposure in middle aged men has been observed following low level lead exposures. An effects threshold for increased blood pressure in men has not been defined; several studies have failed to find one while one longitudinal study suggests of threshold of 30 μg/dl (16).

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## Animal

In experimental animals, effects associated with exposure to lead and lead compounds are similar to those in humans. Observed effects have included weight loss, decreased survival, and neurological, cardiovascular, and kidney effects. Several studies with experimental animals suggest that lead may interfere with the immune response (5).

## Carcinogenicity

### Human

The EPA has classified lead as a Group $B_2$ Carcinogen. Data concerning the carcinogenicity of lead in humans are inconclusive. There is no evidence that oral exposure produces a tumor response. Although studies of occupational inhalation exposure have produced largely negative results, increases in cancer of the digestive organs, respiratory system and kidney have been reported (2,6,19)

### Animal

There is evidence in experimental animals that lead salts are carcinogenic in both mice and rats, resulting in tumors of the kidneys after either oral or parenteral administration. Most of the investigations found a carcinogenic response only at the highest dose. It is unclear how this effect relates to the lower level exposures typical to humans. Metallic lead, lead oxide and lead tetralkyls have not been tested adequately. No studies are available on the carcinogenic potential of lead compounds via inhalation (2).

## Mutagenicity

In a number of DNA structure and function assays, lead has been shown to affect the molecular processes associated with the regulation of gene expression. Lead acetate induces

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cell transformation in Syrian hamster embryo cells and enhances the incidence of simian adenovirus induction. Lead oxide demonstrates a similar enhanced adenovirus induction. Under certain conditions, lead compounds may induce chromosomal aberrations in vivo and in tissue cultures. One study showed a relationship between sister chromatid exchange and lead exposure in exposed workers (2).

## Reproductive Effects

In experimental animals, various non-teratogenic reproductive effects have been observed including developmental delays, decreased fertility, and fetotoxicity. No reproductive effects from human oral exposure to lead have been reported; however, occupational inhalation exposures have been linked to altered testicular function, increases in spontaneous abortion, premature delivery, and early membrane rupture (5).

## Basis for Lead Criteria

The classification of lead as B2, probable human carcinogen, is based on sufficient animal data and insufficient human data. Ten rat bioassays and one mouse assay showed statistically significant increases in renal tumors with dietary and subcutaneous exposure to several soluble lead salts. The most characteristic cancer response is bilateral renal carcinoma, however, there is some evidence of multiple tumor sites (2).

Cancer risk due to exposure to lead involves many uncertainties, such as age, health, nutritional state, body burden and exposure duration which influence the absorption, release and excretion of lead. In addition, current knowledge of lead pharmacokinetics indicates that an estimate derived by standard procedures would not truly describe the potential risk. Therefore, the EPA does not currently recommend a specific cancer potency factor (2).

The water quality criteria of maximum contaminant level goal (MCLG) is based on neurological effects of lead in infants and adverse effects associated with blood lead levels

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of 15 μg/dl. Using a conversion factor of 6.25 to convert from blood lead concentrations to drinking water lead concentrations and an uncertainty factor of 5, the MCLG of 20 μg/l was proposed (2).

The Centers for Disease Control (CDC) has defined an elevated blood lead level for children, which reflects excessive absorption of lead, as a confirmed concentration of lead in whole blood of 25 μg/dl or greater (11). This level is based on several studies. For example, a study of children living near a lead smelter found an erythrocyte protoporphyrin (EP) response at blood lead levels ranging between 10 and 20 μg/dl. Although the biologic threshold for lead toxicity, based on an EP response, is thus less than 20 μg/dl, CDC set the criteria for screening based on several additional factors including acceptability, cost-effectiveness, and the feasibility of effective intervention and follow-up. Thus, the CDC-recommended intervention lead level is 25 μg/dl, associated with an EP level of 35 μg/dl or greater. The CDC is currently reviewing the blood lead level of concern; the guideline is expected to be revised downward, but it is unclear whether CDC will consider the distinction between blood lead levels associated with prenatal, and, hence, maternal exposures and those associated with post-natal exposures. (17).

Risk characterization of lead exposure generally involves using mathematical models to predict blood lead levels that will result from any given range of lead uptake rates. These models allow blood lead levels to be related quantitatively to uptake rates and can provide estimates of the frequency distribution of blood lead levels associated with any given uptake lead exposure scenario.

The Integrated Uptake/Biokinetic (IU/BK) Model, developed for of the U.S. Environmental Protection Agency, accepts either monitoring data or estimated values for the levels of lead in various media. The model predicts mean levels of lead in blood, bone, liver, and kidney for children of different ages. These mean blood lead levels and an estimated geometric standard deviation for blood lead levels in humans can be combined to predict the frequency distribution for population blood lead levels (15).



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The Society of Environmental Geochemistry and Health (SEGH) Task Force has developed a statistical model for estimating acceptable soil lead levels based on a desired mean and range of blood-lead levels. This model utilizes statistical relationships (developed from epidemiological analyses) to describe the contribution of soil sources and non-soil sources to blood lead. Unlike the IU/BK model, the SEGH model does not require the use of assumptions for soil-dust transfer coefficients, soil ingestion rates, and lead bioavailability. Instead, the SEGH model utilizes site-specific environmental health data, such as individual-specific soil lead and blood lead levels, to determine the slope relationship between soil lead and blood lead in the population being studied (18). Once the slope relationship has been established, the frequency distribution of blood lead levels associated with given soil-lead levels can be determined.

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